

June 22, 2004

Thomas M. Gray, M.S., D.A.B.T.
Senior Toxicologist
The American Petroleum Institute
Petroleum HPV Testing Group
1220 L. Street N.W.
Washington, DC 20005

Dear Dr. Gray:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the Aromatic Extracts Category posted on the ChemRTK HPV Challenge Program Web site on January 20, 2004. I commend The American Petroleum Institute Petroleum HPV Testing Group for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that the Group advise the Agency, within 90 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission: Aromatic Extracts Category

Summary of EPA Comments

The sponsor, the American Petroleum Institute, submitted a test plan and robust summaries to EPA for the aromatic extracts category dated December 15, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 20, 2004. The category consists of aromatic substances extracted from lubricating oil basestocks and waxes during petroleum refinement.

EPA has reviewed this submission and reached the following conclusions:

1. Category Definition. The submitter has adequately defined the category.
2. Category Justification. The submitter's support for grouping the chemicals in this category is adequate.
3. Physicochemical Properties. Melting point, boiling point, partition coefficient, and water solubility data are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide more detailed vapor pressure information on representative chemicals.
4. Environmental Fate. Photodegradation, stability in water, and biodegradation data are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide level III fugacity data for these chemicals.
5. Health Effects. (a) *For light paraffinic distillate aromatic extracts (DAEs)*, acute toxicity data are adequate for the purposes of the HPV Challenge Program. EPA reserves judgement on the genetic toxicity endpoint pending receipt of additional information. The submitter needs to conduct a combined repeated-dose reproductive/developmental toxicity screening assay (OECD TG 422) on light paraffinic DAEs. These data can be used to read across to heavy paraffinic DAEs, which are expected to be less bioavailable. (b) *For light naphthenic DAEs*, the submitter needs to conduct acute, repeated-dose, genetic, and reproductive/developmental toxicity testing; one can use a read-across approach to heavy naphthenic DAEs. (c) *For residual aromatic extracts (RAEs)*, repeated-dose toxicity data are adequate for the purposes of the HPV Challenge Program. EPA reserves judgement on the genetic toxicity endpoint pending additional information. For the other endpoints, one can read across from data on DAEs. (d) *For comparisons among all category members*, the submitter needs to provide additional data to demonstrate that toxicity varies with PAC content.
6. Ecological Effects. The data are adequate for the purposes of the HPV Challenge Program.

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.

EPA Comments on the Aromatic Extracts Category Challenge Submission

Category Definition

The category members are byproducts of the solvent extraction of lubricating oil basestocks and waxes. Specifically, they are the solvent extracts of vacuum distillates or vacuum residuum of crude oil that have undergone atmospheric distillation, but not hydrogenation, desulfurization, clay or acid treatment, additional distillation, or solvent extraction.

The category is divided into two subcategories, DAEs and RAEs, based on the vacuum tower fraction from which they are derived. Untreated DAEs are composed of approximately 60%-78% aromatics (consisting of approximately 28%-35% one- or two-ring aromatic hydrocarbons and 17%-23% three- to five-ring aromatic hydrocarbons), with the remainder consisting of naphthenic and isoparaffinic hydrocarbons. Untreated RAEs are composed of approximately 81%-92% aromatics (consisting of approximately 37-40% one- or two-ring aromatic hydrocarbons, 20-23% three- to five-ring aromatic hydrocarbons). RAE's

generally have much higher molecular weights than DAEs, and they generally have long alkyl and naphthene chains:

DAEs

64742-05-8	Extract, distillate, light paraffinic	C ₁₅ -C ₃₀
64742-03-6	Extract, distillate, light naphthenic	C ₁₅ -C ₃₀
64742-04-7	Extract, distillate, heavy paraffinic	C ₂₀ -C ₅₀
64742-11-6	Extract, distillate, heavy naphthenic	C ₂₀ -C ₅₀

RAEs

64742-10-5	Extract, residuum	C ₂₅₊
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The category definition is adequate.

Category Justification

The submitter's rationale for grouping the members into a single category is based on the following:

- Category members are refined by a similar process;
- Their toxicities are proportional to the concentration of dimethyl sulfoxide (DMSO)-extractable three- to seven-ring PACs;
- These PACs are identical in both DAEs and RAEs, although levels that can be extracted are higher in DAEs; and
- Since toxicity is related to DMSO-extractable three- to seven-ring PACs, the data for any one of the four above DAE streams are representative of the entire DAE category.

Although the "Category Rationale" of the test plan did not include an argument for grouping members on the basis of physicochemical or environmental fate properties, information in the test plan suggests a pattern to these properties that is associated with molecular weight.

Comparable health effects data to support the category are limited. In repeated-dose studies, DAEs (levels of paraffins and naphthenes unspecified) and RAEs caused similar effects on hematology, serum chemistry, and organ weight changes. Effects were less severe for RAEs than DAEs, as expected from the lower bioavailability of the larger components. This supports the submitter's read-across strategy from DAEs to RAEs and, by analogy, from light to heavy DAEs. No information was provided to show that testing on paraffinic DAEs would be representative of naphthenic DAEs; thus, EPA recommends testing both groups when there are data gaps.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The data for melting point, boiling point, partition coefficient, and water solubility are adequate.

Vapor Pressure. The submitter provided vapor pressure values of <0.01 hPa for DAEs and RAEs following OECD TG 104. Open-range values do not adequately characterize vapor pressure. The submitter needs to provide data on representative chemicals, as it did for partition coefficient and solubility in different media.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data for photodegradation, stability in water, and biodegradation are adequate.

Fugacity. The level I fugacity data are not adequate. The submitter needs to provide level III fugacity data because the resulting data are more realistic for estimating a chemical's fate in the environment.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

General. For light paraffinic DAEs, acute toxicity data are adequate. EPA reserves judgement on adequacy of the gene mutation data on light paraffinic DAEs pending receipt of clarifying information. The submitter needs to provide further information on or conduct testing for chromosomal aberrations. The DAE used in the oral repeated-dose study was not identified. In addition, only two dose levels were used; therefore, although these data provide some useful information, a true dose-response is not possible. The submitter needs to conduct a combined repeated-dose reproductive/developmental toxicity screening assay (OECD TG 422) on light paraffinic DAEs. These data can be used to read across to heavy paraffinic DAEs.

No data were submitted for light or heavy naphthenic DAEs; the submitter needs to conduct acute, repeated-dose, genetic, and reproductive/developmental toxicity studies on light naphthenic DAEs and use the data to read across to heavy naphthenic DAEs.

For RAEs, repeated-dose toxicity data are adequate. EPA reserves judgement on the genetic toxicity data. Reproductive toxicity and developmental toxicity data are inadequate, but reading across from DAE data is appropriate for these endpoints.

A major part of the submitter's rationale for grouping DAEs and RAEs into a single category is that their toxicity is proportional to their concentration of DMSO-extractable three- to seven-ring PACs. To complete this argument, the submitter needs to provide the following additional information in the test plan and robust summaries:

- The submitter should present data that demonstrate an association between PACs and mammalian toxicity, rather than referring the reader to other sources.
- The PAC content of the test substances should be included in each robust summary.
- Since DAEs and RAEs are characterized by ranges of PACs within the subcategories, those DAEs and RAEs that would be likely to induce toxicity in mammalian species should be identified and characterized.
- Since three- to five-ring PAC's constitute only 17%-23% of the material in DAEs and RAEs, associations between other chemical constituents (aromatic and/or nonaromatic) and DAE- and RAE-induced toxicity should be assessed.

EPA has the following comments on the submitted data.

Acute Toxicity. Oral data on light paraffinic DAEs are adequate, but the submitter needs to conduct an acute toxicity test on a representative light naphthenic DAE, preferably by the oral route. A read-across approach is acceptable for the gap in data on heavy paraffinic and naphthenic DAEs and RAEs.

On page 9 of the test plan, the submitter stated that oral LD₅₀ values for light and heavy DAEs are >5,000 mg/kg; however, this dose is not mentioned in the individual robust summaries.

Repeated-Dose Toxicity. Dermal data on a light paraffinic DAE are inadequate because animals were treated 3 rather than 5 or 7 days/wk. Dermal and oral studies on an unspecified DAE only used two doses, making dose-response evaluation difficult. The submitter needs to conduct new tests, following OECD TG 422, by the oral route on representative light paraffinic and light naphthenic DAEs, since they are expected to be more bioavailable.

Genetic Toxicity. EPA reserves judgement on the bacterial mutagenicity data on DAEs and RAEs because the information came from review articles with insufficient detail. The submitter needs to provide robust summaries for the original studies discussed in the review articles or conduct testing on a representative light naphthenic DAE. EPA also reserves judgement on the mouse lymphoma assay on light paraffinic DAEs because values are reported in conflicting units (nL/mL vs thousands of nL/mL)